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| 10/559,701 | 12/06/2005 | Catherine Abbadie | 21156YP | 1960 |

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| EXAMINER | |
|---|---|
| PAGONAKIS, ANNA | |
| ART UNIT | PAPER NUMBER |
| 1614 | |

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| 12/23/2008 | PAPER |

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/559,701 | ABBADIE ET AL. | |
| | Examiner | Art Unit | |
| | ANNA PAGONAKIS | 1614 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *30 June 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1-5* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-5* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

## DETAILED ACTION

**Claims 1-5 are currently under examination and the subject of this Office Action.**

Applicant's arguments, filed 6/30/2008 have been fully considered. Rejections not reiterated from previous Office Actions are hereby withdrawn. The following rejections are either reiterated or newly applied. They constitute the complete set of rejections presently being applied to the instant application.

### *Claim Rejection - 35 USC § 112, First Paragraph, Scope of Enablement*

### *(New Ground of Rejection)*

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-5 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the treatment of neuropathic pain using the CCR-2 antagonist A, B and C (pages 279-280 of the instant specification), does not reasonably provide enablement for the treatment of the same using any compound found in instant claims 2-3. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

In this regard, the application disclosure and claims have been compared per the factors indicated in the decision *In re Wands*, 8 USPQ2d 1400 (Fed. Cir., 1988) as to undue experimentation. The factors include:

1) the nature of the invention;
2) the breadth of the claims;
3) the predictability or unpredictability of the art;
4) the amount of direction or guidance presented;

5) the presence or absence of working examples;
6) the quantity of experimentation necessary;
7) the state of the prior art; and,
8) the relative skill of those skilled in the art.

The relevant factors are addressed below on the basis of comparison of the disclosure, the claims and the state of the prior art in the assessment of undue experimentation.

The claimed invention is directed to methods of treating neuropathic pain comprising the administration of an effective amount of a CCR-2 antagonist, such as those in instant claims 2-5.

As set forth in *In re Marzocchi et al.,* 169 USPQ 367 (CCPA 1971):

"[A] [s]pecification disclosure which contains teaching of manner and process of making and using the invention in terms corresponding to the scope to those used in describing and defining subject matter sought to be patented must be taken as in compliance with the enabling requirement of first paragraph of 35 U.S.C. 112 *unless there is reason to doubt the objective truth of statements contained therein which must be relied on for enabling support*; assuming that sufficient reasons for such doubt exists, a rejection for failure to teach how to make and/or use will be proper on that basis, such a rejection can be overcome by suitable proofs indicating that teaching contained in the specification is truly enabling." (emphasis added)

The present claims, in the broadest claimed embodiment, circumscribe methods of treating neuropathic pain with use of an effective amount of any of instant compounds of claims 2-5. However, given the data demonstrated in the present disclosure and in consideration of the state of the art at the time of the invention, one of ordinary skill in the art would have been highly skeptical to extrapolate the efficacy shown with CCR-2 antagonists A, B and C to all the compounds of instant claims 2-5.

It is known that neuropathic pain is due to direct peripheral nerve damage, the toxic side effects of drugs, diseases such as diabetes or HIV-infection, inflammation or any combination of these factors (see p. 834, White et al, Nat. Rev. Drug Discovery, 2005, 4: 834-888). The animal models for

neuropathic pain cannot fully represent the complexity of different forms of neuropathic pain in humans. In addition, each animal model of specific neuropathic pain can be only interpreted partially and specifically (see p. 957, conclusions. Wang et al. Adv. Drug. Delivery Rev. 2003, 55: 949-965).

In light of such and, further, given that the art recognizes the highly complex nature and poor understanding of neuropathic pain, the contention that the efficacy shown in treating such a condition using CCR-2 antagonists A, B and C twas reasonably representative of the same or a substantially similar level of efficacy using any other of the instantly claimed CCR-2 antagonists would have been sufficiently unusual that data on a representative number of species would need to be shown demonstrating the reasonable expectation that such efficacy could be properly extrapolated to the larger genus of CCR-2 antagonists. In light of the fact that the treatment of neuropathic pain is highly unpredictable because of its varying etiologies and the efficacy of one therapy is not necessarily suggestive of the same efficacy using a chemically distinct therapy, because the mechanisms behind neuropathic pain are highly complex and elusive, the specification, which lacks an objective showing that the results shown with CCR-2 antagonists A, B and C are suggestive of the same activity of the genus of the instantly claimed as a whole, is viewed as lacking an enabling disclosure.

The specification at pages 279-280 only provides examples directed towards the use of CCR-2 antagonists A, B and C for the treatment of neuropathic pain. The specification, however, lacks any sound scientific reasoning for extrapolating the data shown beyond these three agents as being exemplary for the treatment of neuropathic. In other words, the data shown is not commensurate in scope with the claimed subject matter. Applicant has failed to provide any reasonable basis for extrapolating the results shown from these particular examples to instantly claimed CCR-2 antagonists in general, and how the exemplified species of CCR-2 antagonists A, B and C was reasonably representative of the same level of efficacy of the genus as a whole.

The Examiner acknowledges that the Office does not require the presence of working examples to

be present in the disclosure of the invention (see MPEP §2164.02).

However, in light of the state of the art, which recognizes the unpredictable nature of neuropathic pain, there is no apparent data to support the contention that the use of any of the instantly claimed CCR-2 antagonists would have efficacy in treating the presently claimed disorders, specifically neuropathic pain, since the present specification lacks appropriate disclosure to enable the genus as a whole. Without such direction, a clear burden of undue experimentation would be placed upon the skilled artisan in order to practice the present invention.

In view of the discussion of each of the preceding seven factors, the level of skill in this art is high and is at least that of a medical doctor with several years of experience in the art.

As the cited art and discussion of the above 8 factors establish, practicing the claimed method in the manner disclosed by Applicant would not imbue the skilled artisan with a reasonable expectation that the treatment of the presently claimed disorders, specifically neuropathic pain, could be achieved using any CCR-2 antagonists other than CCR-2 antagonists A, B and C, given the disclosure and the supporting examples provided in the present specification.

**Conclusion**

Any inquiry concerning this communication or earlier communications from the examiner should be directed to ANNA PAGONAKIS whose telephone number is (571)270-3505. The examiner can normally be reached on Monday thru Thursday, 9am to 5pm EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin H. Marschel can be reached on 571-272-0718. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

AP

/Ardin Marschel/
Supervisory Patent Examiner, Art Unit 1614